IN THE U.S. PATENT AND TRADEMARK OFFICE

Applicant:	ZAVIALOV et al.	Conf.:	7527
Appl. No.:	09/424,080	Group:	1646
Filed:	February 14, 2000	Examiner:	J. Andres

For: COMPOSITIONS FOR ENHANCING IMMUNOSUPPRESSANTS' PHARMACEUTICAL ACTIVITIES

#13
8/15/01

REPLY TO RESTRICTION REQUIREMENT

Assistant Commissioner for Patents
Washington, DC 20231

August 13, 2001

Sir:

In reply to the Restriction Requirement dated June 13, 2001, the due date for responding having been extended for one month to August 13, 2001, the following remarks are respectfully submitted in connection with the above-identified application.

REMARKS

Claims 1 and 3-18 are pending in the present application.

The Examiner has restricted the subject matter of the claims into the following two groups of species.

Group I - Immunosuppressants

a) cyclosporins

b) FK 506; and

c) rapamycin

Group II - bioactive peptides

a) α-peptoferin

b) albeferon

c) albebetin; and

d) mixtures thereof.

The Examiner requires that Applicant elect one species of each group for examination. The Examiner bases this restriction on the assertion that the species are not so linked as to form a single general inventive concept. Applicants traverse this restriction and withdrawal thereof is respectfully requested.

The present invention is drawn to a composition of immunosuppressants and bioactive peptides. Contrary to the assertion of the Examiner the immunosuppressants of Group I share a common inventive concept, as do the bioactive peptides of Group II. The common inventive concept associated with the compositions of the present invention is the diminishing of the undesirable side effects associated with the immunosuppressants of Group I.

Cyclosporins, FK506, and rapamycin are all microbial cyclic peptides that are used as immunomodulatory drugs. All of these

immunosuppressant peptides possess unusual or modified amino acids and all have the shared structure of an active site that binds to peptidyl-prolyl cis/trans isomerase (binding region) and an effector site that binds to calcineurin or the FRAP receptor. FK506 is the smallest of the class of drug molecules, rapamycin is of intermediate size and cyclosporin is the largest. However, despite the differences in size these molecules all have the same active site and effector region structure and the distance between the sites does not matter for activity. Attached hereto are journal articles that discuss the molecular mechanism activity of the compounds of Group I. The APMIS article discusses the molecular mechanism of the cyclosporin, CyA. The article from Computers Chem. discusses the similarities between the structures of the three drugs. Applicants note one point that the mechanism of rapamycin discussed in the Introduction section of the Computers Chem. article is not completely correct because there is some difference between rapamycin and CyA, but not as much as previously thought. In summary, the immunosuppressants of Group I share common active sites and effector sites and therefore mechanisms for activity.

The bioactive peptides also share the common feature of comprising the amino acids from the active site of interferons and

have been obtained by sequence alignment from various organisms. See page 9, final paragraph, spanning page 10. The differences in sequences are minor and inconsequential with respect to the activity of the peptides in the present invention as all of the peptides share a common activity. Thus, the bioactive peptides of Group II all act by a common mechanism to reduce the side effects associated with the immunosuppressants of Group I, that is the bioactive peptides have a synergistic effect with the immunosuppressants and amplify their activity, thus decreasing the doses of the immunosuppressants that are needed and the concomitant harmful side effects. Thus, the species of Group I all share a common inventive concept as do the species of Group II. Withdrawal of the restriction is therefore respectfully requested.

Should the Examiner choose not to withdraw the restriction, Applicants elect with traverse cyclosporins from Group I and α-peptoferon from Group II.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact MaryAnne Armstrong, Ph.D. (Reg. No. 40,069) at the telephone number of the undersigned below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

Pursuant to 37 C.F.R. §§ 1.17 and 1.136(a), Applicant(s) respectfully petition(s) for a one (1) month extension of time for filing a reply in connection with the present application, and the required fee of $55.00 is attached hereto.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17; particularly, extension of time fees.

Respectfully submitted,

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